

Hydrophobically modified polymers can minimize skin irritation potential caused by surfactant-based cleansers

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Summary

Introduction The addition of hydrophobically modified polymers (HMPs) to cleansers that contain surfactants can create polymer–surfactant complexes that are less irritating to the skin than commercially available mild cleansers. Our objective was to compare the tolerability and efficacy of a test foaming liquid facial cleanser containing HMPs with a commercial liquid nonfoaming facial cleanser in women with sensitive skin.

Methods In this randomized, prospective, double-blind, comparative study, women ($n = 20$ per group) with mild-to-moderate atopic dermatitis (AD), eczema, acne, or rosacea used a test gentle foaming liquid facial cleanser containing HMPs or a commercial gentle liquid nonfoaming facial cleanser daily for 3 weeks. Investigators assessed irritation and skin condition. Study subjects also assessed their skin properties and the performance of each cleanser.

Results Clinicians as well as study subjects consistently rated the test cleanser as effective or slightly more effective at improving symptoms than the commercial cleanser, although no significant differences between groups were observed. At weeks 1 and 3, respectively, more users of the commercial cleanser reported irritation (20% and 10%) than users of the test cleanser (5% and 5%). In addition, subject self-assessments of skin condition and cleansing properties were slightly more improved with the test cleanser than with the commercial cleanser.

Conclusions Both the test foaming cleanser containing HMPs and the commercial nonfoaming cleanser were effective and well accepted by most women in the study. Improvements were observed by both clinicians and subjects in the group using the test cleanser containing HMPs in all evaluated skin categories.

Keywords: acne, atopic dermatitis, cleanser, eczema, irritation, skin, surfactant, tolerance

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Introduction

Nearly all modern body cleansers contain at least one surfactant, or surface-acting agent, a class of molecules that have hydrophilic and hydrophobic domains.¹ Surfactant's unique chemistry enables the solubilization of hydrophobic compounds present in oils, dirt, sebum, and other unwanted substances from skin, allowing these materials to be washed away with greater ease than what could be achieved with water

alone.^{2,3} Several classes of surfactants are used in facial cleansers, including anionic surfactants (e.g., sodium lauryl sulfate [SLS] and sodium laureth sulfate [SLES]), amphoteric surfactants (e.g., cocamidopropyl betaine), and nonionic surfactants (e.g., alkyl polyglucoside).³

The foaming action and mildness of a cleanser are influenced by surfactant charge, and the formation of spherical structures called micelles that help dissolve and remove oil and lipids from skin.^{1–3} Surfactant selection represents a trade-off between functionality, esthetics, and mildness. For example, anionic and amphoteric surfactants are effective emulsifying and foaming agents, but in certain instances, they are less mild than nonionic surfactants and may have the potential to cause irritation.^{3,4} Furthermore, surfactants can penetrate through the stratum corneum (SC) and interact with proteins and lipids in the epidermis,⁵ resulting in skin tightness, skin dryness, epidermal barrier damage, erythema, irritation, and itching.^{3,6–9}

In those with atopic dermatitis (AD), use of a cleanser with traditional surfactants can exacerbate the disease, leading to a loss of intracellular lipids and skin with a red, scaly appearance. Further damage to skin in those with AD can lead to exposure of dermal nerve endings and itching, burning, and pain.¹⁰ Facial rosacea is also associated with an overly permeable skin barrier, and as a result, these individuals have a lower tolerance to many skin care products and cosmetics.¹⁰ For these reasons, gentle skin cleansing is of particular importance to adults with acne, atopic dermatitis, eczema, rosacea, or other dermatologic conditions associated with compromised skin barrier integrity.^{1–3,10}

Early soaps consisted of the salts of fatty acids and were derived from plant or animal triglycerides in combination with base, typically lye. Although soaps are effective cleansers, alkaline soaps can increase skin surface pH¹¹ and can dissolve fat-soluble and water-soluble components from the surface of skin.¹² Because of these properties, alkaline cleansers have greater potential to irritate skin than neutral cleansers^{11,13,14} and can adversely affect the skin's barrier repair mechanism.¹⁰ Liquid detergents enable the creation of liquid surfactant solutions at pHs below seven and enable less damage and drying of the skin. Addition of cationic polymers to skin cleansers can further protect the skin and improve moisturization.^{1–3} To further improve cleanser mildness, adding hydrophobically modified polymers (HMPs) to cleansers that contain surfactants can help to create polymer–surfactant complexes that are even less irritating to the SC lipid barrier.^{1,15,16} HMPs interact with the hydrophobic tails of other surfactants, leading to the formation of larger surfactant structures and a

reduction in the surfactant dynamics. HMPs also lower the effective concentration of free surfactant micelles in solution and facilitate foam formation.¹⁶

In this study, we describe the results of a clinical study that tested the tolerance and efficacy of a facial cleanser with HMPs against a gentle nonfoaming commercial facial cleanser. The goal of the study was to investigate and compare the tolerability of these cleansers in women with sensitive skin (e.g., AD, eczema, rosacea, or acne) as well as to evaluate efficacy of the cleansers to remove facial dirt, cosmetics, and sebum.

Materials and methods

This was a randomized, prospective, double-blind, comparative study designed to assess the tolerability and efficacy of a test liquid gentle foaming facial cleanser compared to a commercial liquid gentle nonfoaming facial cleanser commonly recommended by dermatologists. Female subjects were recruited from a private practice database of patients who possessed the desired dermatologic conditions required for entry into this sensitive skin study. The study protocol was approved by an independent ethics committee and was conducted in compliance with the current standards and principles of the Declaration of Helsinki and the International Conference on Harmonization Guideline for Good Clinical Practice. Prior to enrolling in the study, all women provided written informed consent. The subjects were compensated for their travel and time at the rate of \$50 per visit for each completed visit.

Healthy female adults (aged 18–65 years) with mild-to-moderate AD, eczema, acne, or rosacea within the previous 90 days (assessed by a dermatologist) were eligible to participate in the study. Mild-to-moderate AD was defined as atopy (hay fever, asthma, or eczema), recurrent dermatitis (past or present), recurrent itching, and history of recurrent dermatitis in the flexural areas within the previous 90 days. In the absence of any of the symptoms named above, AD was also diagnosed if at least two of the following conditions were present: onset of disease during infancy; nipple dermatitis; condition worsens with sweating or stress; recurrent hand dermatitis (past or present); cheilitis; allergies to food, pets, or pollen; or skin easily irritated by any of the following: soaps, detergents, household cleansers, solvents, cosmetics, or perfumes/fragrances.

Mild-to-moderate active rosacea was defined as having 3–4 inflammatory papules and mild-to-moderate erythema within the previous 90 days. Mild-to-moderate active eczema was defined as having mild-to-moderate

dryness, scaling, and erythema within the previous 90 days. Mild-to-moderate active acne was defined as having a minimum of 3–4 inflammatory papules and 10 noninflammatory comedones within the previous 90 days. Women were required to continue their normal course of treatment for preexisting conditions throughout the study, substitute the assigned product for their usual facial cleanser for the duration of the study, and use birth control during the study (if needed). If a woman was using an oral or topical medication at the beginning of the study, no restrictions were placed on her use of the medication.

Women were excluded from the study if they met any of the following conditions: occurrence of skin disease other than AD, eczema, rosacea, or acne; occurrence of other medical conditions that might interfere with skin evaluations; occurrence of disease that might pose a risk to participating panelists; occurrence of clinically significant unstable medical disorder; use of topical therapy or medication other than hydrocortisone or triamcinolone 0.1% cream within 96 h of the study; pregnancy or intention to become pregnant; active lactation; participation in another study or trial ≤ 30 days prior to enrolling in the study; use of an indoor tanning booth; unwilling or unable to comply with the requirements of the study protocol.

The study took place in a dermatology clinic and the routine setting of a woman's home. Participating women were divided equally into two groups. During randomization, study participants were stratified and balanced for demographics and the presence and severity of acne, eczema, rosacea, and atopic dermatitis. Women in each group were instructed to use their assigned liquid facial cleanser at least once daily for 3 weeks and to apply the cleanser to the face only and avoid the eye and mouth. Specifically, subjects were asked to wash their face with the provided test cleanser and then pat their face dry. They were allowed to use any nonmedicated facial moisturizer and normal-colored facial cosmetics. Subjects were reminded to not change their normal moisturizer or cosmetics during the study.

They were instructed not to share the test products with other household members. Study participants kept diaries that were collected and reviewed during each study visit. Diaries were used to insure that study participants were compliant and were using the facial cleanser as directed. Participants visited the study clinic at baseline and after weeks 1 and 3.

In this report, we describe the results from women who received a test liquid gentle foaming facial cleanser or a benchmark commercial gentle nonfoaming facial cleanser commonly recommended by der-

matologists. The test foaming facial cleanser contained the HMP potassium acrylates copolymer, glycerin, and a surfactant system primarily containing cocamidopropyl betaine and lauryl glucoside (Neutrogena Ultra Gentle Gel Cleanser; Neutrogena Corp. Los Angeles CA, USA) prepared without fragrance. The commercial nonfoaming facial cleanser did not contain HMP (Cetaphil® Gentle Skin Cleanser; Galderma Laboratories, L.P., Fort Worth, TX, USA).

The primary endpoint of the study was the investigator-assessed presence or absence of facial irritation attributes (e.g., stinging, erythema, burning) or the worsening of eczema, atopic dermatitis, acne, or rosacea after 3 weeks of liquid facial cleanser use. Secondary endpoints included the investigator-led assessment of facial dirt removal and the removal of cosmetics and sebum following the use of each facial cleanser. Clinicians also evaluated facial skin softness, smoothness, irritation, erythema, and desquamation at each study visit. The presence of comedones and clogged pores was assessed for comedogenic potential of the cleansers. Global disease severity was visually rated by the dermatologist investigator as an overall assessment of skin condition independently from the other evaluation criteria. Facial skin attributes were assessed by clinicians using a five-point ordinal scale (Table 1). Ordinal scores at baseline and weeks 1 and 3 were used to calculate the percent change in facial skin attributes at weeks 1 and 3 from baseline. Direct comparisons between the facial cleansers were made throughout the study to evaluate and compare the relative performance of each cleanser.

In addition to clinician assessments, study participants also assessed their skin and the performance of each facial cleanser throughout the study. The participants were asked to agree or disagree with specific statements about the efficacy of each facial cleanser at the 1- and 3-week time points. They also assessed facial cleanser tolerability and the change in symptoms associated with eczema, atopic dermatitis, acne, or rosacea

Table 1 Clinician and subject assessment scoring

Evaluator	Classification	Score
Clinician	None	0
	Minimal	1
	Mild	2
	Moderate	3
	Severe	4
Subject	None	0
	Minimal	1
	Good	2
	Excellent	3
	Superior	4

throughout the study. They evaluated skin softness, smoothness, cleanliness, rich lather, overall cleansing experience, radiance, and the removal of facial dirt, cosmetics, and sebum. The women participants used an ordinal evaluation scale for self-assessments (Table 1). Similar to the clinician assessment data, ordinal scores at baseline and weeks 1 and 3 were used to calculate percent change (percent improvement) from baseline.

Direct comparisons between facial cleansers were made throughout the study to evaluate participants' opinions about the performance of each cleanser. The change (percent improvement) in ordinal scores at weeks 1 and 3 from baseline and direct comparisons between the cleansers were tested for statistical significance using a two-tailed Mann–Whitney U nonparametric test, and statistical significance was set at $P \leq 0.05$.

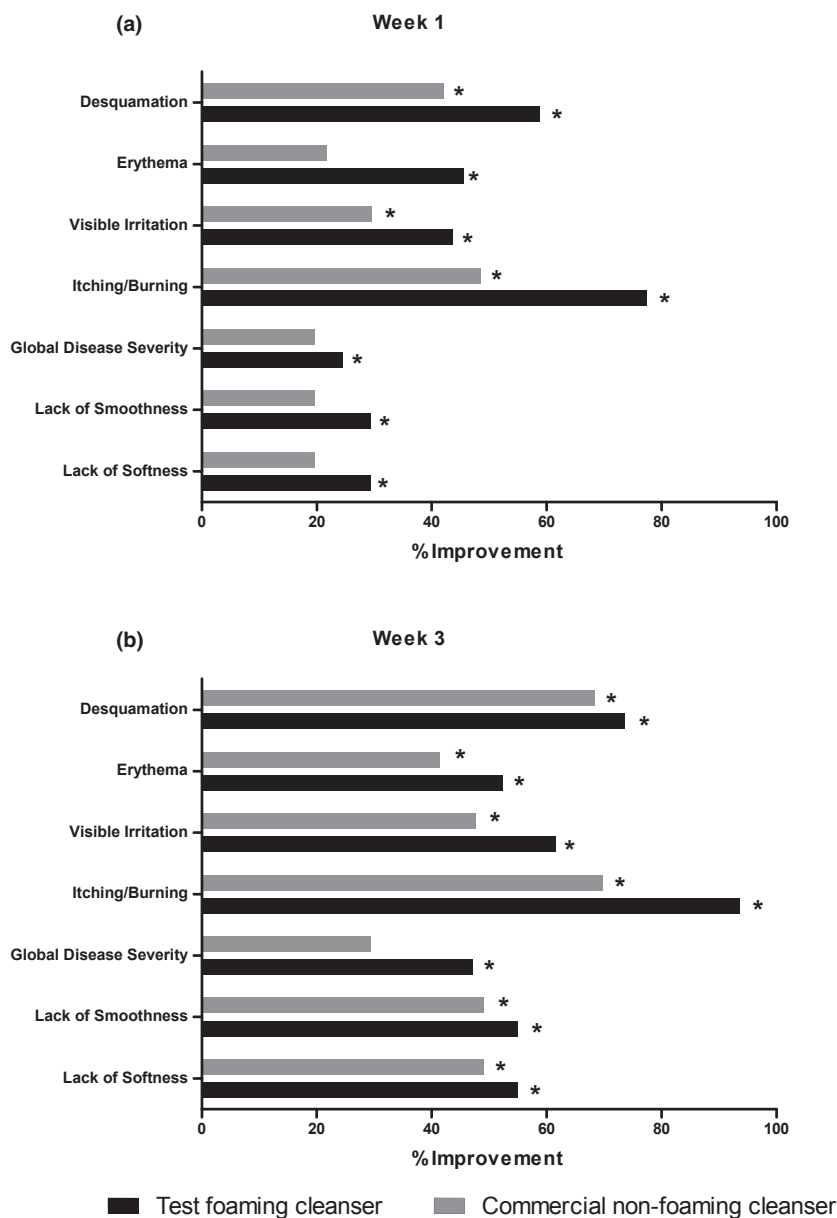


Figure 1 Clinical assessment of test gentle foaming cleanser and commercial nonfoaming facial cleanser after week 1 (a) and week 3 (b). Data are shown as the percent improvement from baseline in mean ordinal scores. * $P < 0.05$ vs. baseline. No significant differences between groups were noted for any category.

Adverse events (AEs) and serious adverse events (SAEs) were recorded and monitored throughout the study.

Results

All enrolled participants ($n = 20$ per group) completed the study. Clinician assessment data for facial skin attributes following facial cleanser use are shown in Figure 1. Use of the test foaming facial cleanser for 1 and 3 weeks led to a significant improvement from baseline ($P < 0.05$) in all categories tested (skin softness, skin smoothness, global disease severity, itching/burning, visible irritation, erythema, and desquamation). The percent improvement appeared greater for itching/burning and desquamation than in the other tested categories. In the women using the commercial nonfoaming facial cleanser, significant positive changes from baseline at week 1 were noted only for itching/burning, visible irritation, and desquamation ($P < 0.05$), while at week 3, significant improvements from baseline were noted for all categories except global disease severity ($P = 0.06$). After 3 weeks, use of either type of facial cleanser generally led to more improvement from baseline in skin softness, skin smoothness, global disease severity, itching/burning, visible irritation, erythema, and desquamation than were observed after 1 week. At all time points and overall categories measured, women using the test foaming cleanser containing HMP appeared to exhibit greater improvement than those using the gentle commercial nonfoaming

cleanser, although there were no statistically significant differences between the groups.

After 1 week, facial irritation was observed in 20% of women using the commercial nonfoaming facial cleanser and in 5% of those using the test foaming HMP cleanser (Fig. 2). At week 3, 10% of the commercial nonfoaming facial cleanser users and 5% of the subjects in the group with the test foaming HMP cleanser reported facial irritation.

As part of the study, women were asked to agree or disagree with specific statements about the efficacy of each facial cleanser at the 1- and 3-week time points. As shown in Figure 3, most women agreed with the statements after using the benchmark commercial nonfoaming cleanser or the test foaming facial cleanser for 1 week or 3 weeks. Of note, 80% or more of women agreed with each statement about the effectiveness of the test facial cleanser with HMPs at week 1 and more than 90% agreed at week 3. The majority of women who used the commercial nonfoaming facial cleanser also agreed with each statement, with more than 70% agreeing at week 1 and more than 78% at week 3.

In addition, the women reported that the use of either facial cleanser for 1 week or 3 weeks led to a statistically significant ($P < 0.001$) improvement from baseline in skin condition, smoothness, softness, cleanliness, radiance, and cleansing satisfaction, with no significant differences between groups (Fig. 4). As expected, more women reported lathering in the test facial cleanser with HMPs group than in those using the nonfoaming facial cleanser ($P < 0.001$).

In the group that received the test foaming facial cleanser with HMPs, there was one report of “did not remove eye cosmetics”, and one report of “poor facial cleansing”. In the group that received the commercial nonfoaming facial cleanser, there was one report each of “no lather”, “does not feel clean”, “poor facial cleansing”, and “lathers poorly”. There was no evidence that the cleansers were comedogenic.

No safety-related AEs or SAEs were reported during the study. There was one report of facial tightness in each treatment group.

Discussion

In this study, both facial cleansers were well tolerated and demonstrated high acceptability among these women with sensitive skin. Clinicians rated various clinical aspects of skin conditions, such as erythema, irritation, global disease severity, smoothness, and softness, and consistently rated the test foaming cleanser

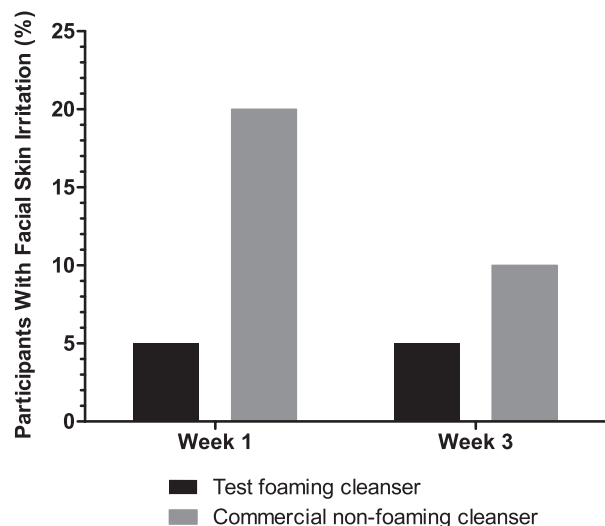


Figure 2 Percentage of study participants with irritation at week 1 and week 3.

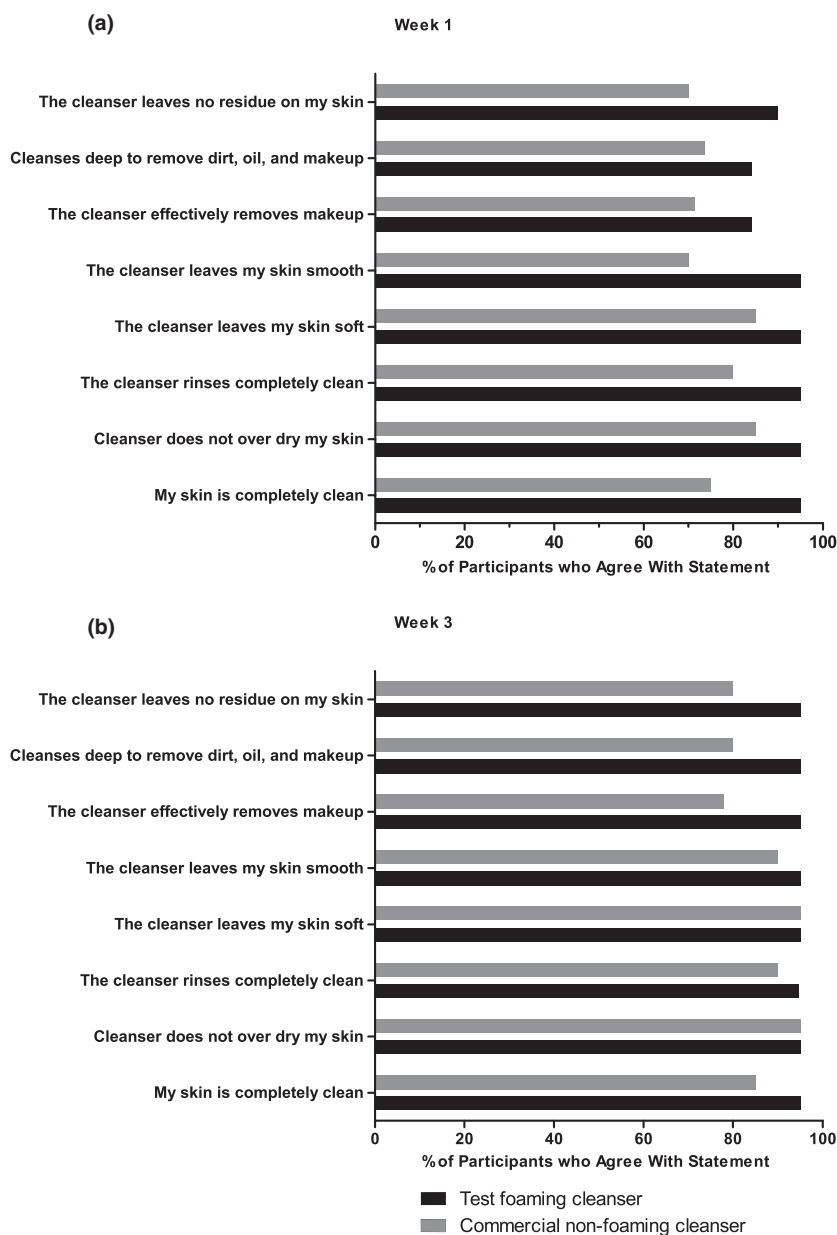


Figure 3 Participant agreement with statements about cleansing efficacy and makeup removal at week 1 (a) and week 3 (b).

with HMP to effectively improve symptoms at both the 1- and 3-week (primary endpoint) test periods. Irritation was reported by more users of the commercial nonfoaming cleanser than was reported by users of the test foaming cleanser with HMP. The subjects performed self-assessments that evaluated different endpoints. Self-assessment scores related to cleansing properties and improvements in skin characteristics were greater with the test foaming cleanser than with the commercial nonfoaming cleanser, although the

differences were not statistically significant. These results indicated that the test cleanser with HMP was able to significantly improve clinician assessment of skin attributes from baseline values, effectively perform as a cleanser, and provide adequate lather. It also appeared to be as tolerable as the commercial nonfoaming cleanser.

Cleanser-induced irritation, skin tightness, and skin dryness are all associated with impaired skin barrier properties and penetration of surfactants into the

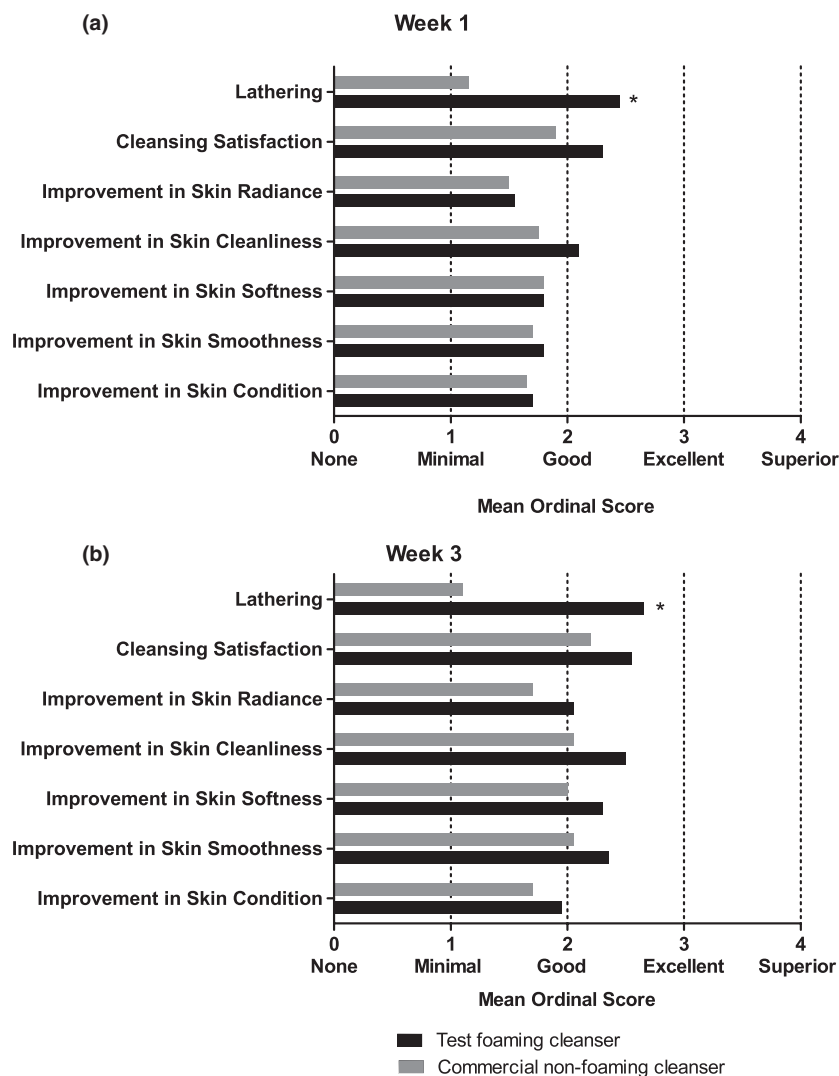


Figure 4 Mean participant assessment score for test foaming and commercial nonfoaming facial cleanser after 1 week (a) or 3 weeks (b). Change from baseline for each parameter tested was statistically significant in both groups. * $P < 0.001$ vs. commercial nonfoaming facial cleanser.

SC.^{1,3,10,17} Mild moisturizing cleansers are expected to provide cleansing benefits without negatively altering the hydration and viscoelastic properties of skin.³ Formulators can use combinations of surfactants to create cleansers that are milder, which may be particularly ideal for individuals with AD.^{1,16} For example, facial cleansers containing a blend of anionic and amphoteric surfactants can be formulated to be milder than cleansers containing a weight-equivalent proportion of anionic surfactant.¹⁸ Although gentle facial cleansers are effective at cleansing and removing makeup and other unwanted substances from skin, they are ineffective at generating foam, which may be less preferred by consumers.¹⁶

In addition to reducing the extent of surfactant penetration into the skin and thus reducing the potential for skin irritation,¹⁶ HMPs and HMP–surfactant complexes are surface active and can improve foaming by stabilizing the air–water interface of bubbles.¹⁶ In this way, HMP addition to surfactant-containing cleansers can both reduce the potential for skin irritation and improve foam and lather, a quality usually associated with traditional soaps. The ability to combine low irritation potential with foaming is a positive attribute of HMP-containing cleansers.

In conclusion, the test foaming cleanser with HMPs offers a new cleansing option for adults with sensitive

skin. The test foaming facial cleanser with HMPs was effective and well accepted by most women in the study. The improvements in the evaluated skin categories that were reported by both clinicians and subjects using the test foaming facial cleanser were comparable to those observed in the subjects using the commercial nonfoaming cleanser.

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